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### Search Strategy

FILE 'USPATFULL' ENTERED AT 18:53:41 ON 12 JUN 2003

E ALIZON MARC/IN  
L1 49 S E3  
L2 29 S L1 AND (HIV-2 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 2)  
L3 29 S L2 AND (POL)  
L4 4 S L3 AND (POL/CLM)  
L5 2735 S (HIV-2 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 2)  
L6 949 S L5 AND (POL)  
L7 120 S L6 AND (POL/CLM)  
L8 116 S L7 NOT L1

FILE 'WPIDS' ENTERED AT 19:01:33 ON 12 JUN 2003

E ALIZON MARC/IN  
L9 16 S E2  
L10 7 S L9 AND (HIV-2 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 2)  
L11 1 S L10 AND (POL)

FILE 'MEDLINE' ENTERED AT 19:02:36 ON 12 JUN 2003

E ALIZON M/AU  
L12 67 S E3 OR E4  
L13 14 S L12 AND (HIV-2 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 2)  
L14 3580 S (HIV-2 OR HUMAN IMMUNODEFICIENCY VIRUS TYPE 2)  
L15 161 S L14 AND POL  
L16 111 S L15 AND (NUCLEIC ACID OR NUCLEOTIDE SEQUENCE OR GENE OR PROBE)  
L17 0 S L16 AND PY=1985  
L18 0 S L16 AND PY=1986  
L19 2 S L16 AND PY=1987  
L20 8 S L16 AND PY=1988

L4 ANSWER 2 OF 4 USPATFULL

2002:51108 CLONED DNA SEQUENCES RELATED TO THE ENTIRE GENOMIC RNA OF HUMAN IMMUNODEFICIENCY VIRUS II (HIV-2), POLYPEPTIDES ENCODED BY THESE DNA SEQUENCES AND USE OF THESE DNA CLONES AND POLYPEPTIDES IN DIAGNOSTIC KITS.

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Institut Pasteur, Paris, FRANCE (non-U.S. corporation)  
US 6355789 B1 20020312  
APPLICATION: US 1995-468424 19950606 (8)  
PRIORITY: FR 1986-911 19860122  
FR 1986-1635 19860206  
FR 1986-1985 19860213  
FR 1986-3881 19860318  
FR 1986-4215 19860324

DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed toward nucleic acids containing the full-length human immunodeficiency virus type 2 ROD (HIV-2.sub.ROD) pol gene. HIV-2, which was originally designated lymphadenopathy-associated virus type II (LAV-II), was isolated from AIDS patients in West Africa. The virus is genotypically and phenotypically distinct from HIV-1 and bears a closer genetic relationship to the simian immunodeficiency virus (SIV). The present invention describes the preparation of HIV-2.sub.ROD proviral molecular clones from a genomic lambda phage library of CD4.sup.+/-infected cells. The complete nucleotide sequence of the full-length genome was determined and the putative gag, pol, env, vif (Q), vpr (R), vpx (X), nef (F), tat, and rev (art) genes identified. The claimed invention is directed toward nucleic acids containing the full-length HIV-2.sub.ROD pol gene (nt 1829-4936). These nucleic acids should prove useful as diagnostic reagents for the detection of HIV-2 and facilitate expression of the pol gene product.

CLM What is claimed is:

1. A nucleic acid of HIV-2 having the nucleotide sequence of a full length pol gene as set forth in FIG. 6.

L13 ANSWER 12 OF 14 MEDLINE

87173056 Document Number: 87173056. PubMed ID: 3031510. Genome organization and transactivation of the human immunodeficiency virus type 2.  
Guyader M; Emerman M; Sonigo P; Clavel F; Montagnier L; Alizon M  
. NATURE, (1987 Apr 16-22) 326 (6114) 662-9. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Analysis of the nucleotide sequence of the human retrovirus associated with AIDS in West Africa, HIV-2, shows that it is evolutionarily distant from the previously characterized HIV-1. We suggest that these viruses existed long before the current AIDS epidemics. Their biological properties are conserved in spite of limited sequence homology; this may help the determination of the structure-function relationships of the different viral elements.

L13 ANSWER 14 OF 14 MEDLINE

87090385 Document Number: 87090385. PubMed ID: 3025743. Molecular cloning and polymorphism of the human immune deficiency virus type 2. Clavel F; Guyader M; Guetard D; Salle M; Montagnier L; Alizon M. NATURE, (1986 Dec 18-31) 324 (6098) 691-5. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB We recently reported the isolation of a novel retrovirus, the human immune deficiency virus type 2 (HIV-2, previously named LAV-2), from patients with acquired immune deficiency syndrome (AIDS) originating from West Africa. This virus is related to HIV-1, the causative agent of the AIDS epidemic now spreading in Central and East Africa, as well as the USA and Europe (see ref. 3 for review) both by its morphology and by its tropism and in vitro cytopathic effect on CD4 (T4) positive cell lines and lymphocytes. But preliminary hybridization experiments indicated that there are substantiated differences between the sequences of the two genomes. Furthermore, the proteins of HIV-1 and HIV-2 have different sizes and their serological cross-reactivity is restricted to the major core protein, as the envelope glycoproteins of HIV-2 are not immunoprecipitated by HIV-1-positive sera. We now report the molecular cloning of the complete 9.5-kilobase (kb) genome of HIV-2, the observation of restriction site polymorphism between different isolates, and a preliminary analysis of the relationship of HIV-2 with other human and simian retroviruses.

L19 ANSWER 1 OF 2 MEDLINE

87299191 Document Number: 87299191. PubMed ID: 3040052. Genetic analysis of a new subgroup of human and simian T-lymphotropic retroviruses: HTLV-IV, LAV-2, SBL-6669, and STLV-IIIAGM. Franchini G; Collalti E; Arya S K; Fenyo E M; Biberfeld G; Zagury J F; Kanki P J; Wong-Staal F; Gallo R C. AIDS RESEARCH AND HUMAN RETROVIRUSES, (1987 Spring) 3 (1) 11-7. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB A new primate retrovirus, STLV-IIIAGM, has been recently isolated from healthy African green monkeys and is apparently nonpathogenic in its natural host. However, spontaneous infection as well as inoculation of STLV-IIIAGM into macaques induces a disease with clinical features that resemble human AIDS. Independent isolates of human retroviruses, serologically closely related to STLV-IIIAGM, have been obtained from healthy individuals (HTLV-IV) and patients with immunodeficiency (LAV-2FG and SBL 6669) from West Africa. The latter have also been referred to as HIV-2 because, like HTLV-III/HIV-1, they may be associated with immune deficiency, or as West African human retroviruses because of their prevalence and probable origin from that region. We have molecularly cloned the STLV-IIIAGM genome and have generated probes from the gag-pol and envelope genes to analyze the genetic relatedness of these simian and human retroviruses. Our results indicate that all these retroviruses are genetically closely related to each other; HTLV-IV and STLV-IIIAGM differing only by a few restriction enzyme sites while LAV-2FG and SBL 6669 exhibit greater polymorphism from HTLV-IV/STLV-IIIAGM. These data mirror the variable degree of relatedness among members of the first subgroup of human retroviruses, HTLV-III/HIV.

L20 ANSWER 1 OF 8 MEDLINE

89126935 Document Number: 89126935. PubMed ID: 2464734. Molecular evolution of the human and simian immunodeficiency viruses. Yokoyama S. (University of Illinois, Urbana-Champaign 61820. ) MOLECULAR BIOLOGY AND EVOLUTION, (1988 Nov) 5 (6) 645-59. Journal code: 8501455.

ISSN: 0737-4038. Pub. country: United States. Language: English.

AB Molecular evolution and phylogeny of different human immunodeficiency virus type 1 (HIV1) strains, of a type 2 (HIV2) strain, and of two simian immunodeficiency viruses (SIVAGM and SIVMAC) have been studied by comparing the nucleotide sequences of the two regions of their pol genes which encode the reverse transcriptase (RT) and endonuclease/integrase (EN). The analyses show that the different HIV 1s form one cluster (HIV1 group) and that the SIVs and HIV2 form another (HIV2 group). When the entire genomes of a HIV1, a HIV2, and the two SIVs were compared, the SIVAGM showed a unique pattern of mutation accumulations; that is, the SIVAGM has accumulated more nonsynonymous changes than synonymous changes in the RT and EN regions after its recent divergence from SIVMAC-142, and, furthermore, it has a deletion of approximately 350 bp in the region between the pol and env genes. The SIVAGM was apparently derived from cell cultures infected with a macaque isolate, SIVMAC-251. The contamination provides an opportunity to measure the maximum rate of evolution in the SIVAGM by comparing its DNA sequence to those of SIVMAC-251 and SIVMAC-142. The analysis shows that the rates are given approximately by  $(1.95 \pm 1.37) \times 10^{-3}$ /site/year for one SIVAGM sequence and  $(5.18 \pm 2.25) \times 10^{-3}$ /site/year for another.

L20 ANSWER 3 OF 8 MEDLINE

89078628 Document Number: 89078628. PubMed ID: 2462515. Predictions of linear T-cell and B-cell epitopes in proteins encoded by HIV-1, HIV-2 and SIVMAC and the conservation of these sites between strains. Zvelebil M J; Sternberg M J; Cookson J; Coates A R. (Department of Crystallography, Birkbeck College, London, England. ) FEBS LETTERS, (1988 Dec 19) 242 (1) 9-21. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB An important consideration in the design of vaccines to prevent HIV-1 infection effective against different strains is the amino acid sequence conservation of antigenic determinants. Even one amino acid change can destroy the antigenicity of a site for the antibody or T-cell receptor. The comparisons of predicted T- and B-cell epitopes between human HIV-1, HIV-2 and monkey SIVMAC AIDS viruses are presented. The three major gene products (env, gag and pol) were examined. A number of epitopes were identical between strains of HIV-1. Our analysis highlights the problem of designing an effective HIV-1 and HIV-2 vaccine and also the problem of testing human vaccines in monkey models.

L20 ANSWER 8 OF 8 MEDLINE

88230619 Document Number: 88230619. PubMed ID: 2453682. A single 66-kilodalton polypeptide processed from the human immunodeficiency virus type 2 pol polyprotein in Escherichia coli displays reverse transcriptase activity. Le Grice S F; Zehnle R; Mous J. (Central Research Units, F. Hoffmann-LaRoche & Co. Ltd., Basel, Switzerland. ) JOURNAL OF VIROLOGY, (1988 Jul) 62 (7) 2525-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB We have cloned the entire pol gene of human immunodeficiency virus type 2 into a high-level Escherichia coli expression system. Induction of cultures containing the recombinant plasmid, p2RTL1, leads to rapid accumulation of polypeptides of 66, 54, and 34 kilodaltons. We have designated the larger polypeptides reverse transcriptase, and we have designated the smaller polypeptide endonuclease. Purification of reverse transcriptase via

ion-exchange and affinity chromatography yields the 66-kilodalton polypeptide, with which reverse transcriptase activity is associated. Purified enzyme furthermore displays a higher apparent molecular weight than its counterpart from human immunodeficiency virus type 1.

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#### NOTES

- Disclosure provides full-length *pol* gene and a single fragment corresponding to nt 991-1053. No other *pol* fragments or sequences are described.